Modern Concepts of Cardiovascular Disease

Published monthly by the AMERICAN HEART ASSOCIATION
44 EAST 23RD STREET, NEW YORK 10, NEW YORK

Vol. XXIX **SEPTEMBER, 1960** **No. 9**

IDIOPATHIC PERICARDITIS*

This discussion concerns the form of pericardial disease generally referred to as "idiopathic" or "nonspecific." Additional adjectives, such as "benign" or "acute," are commonly used for further qualification. Semantically, the favored term of benign idiopathic pericarditis is particularly unfortunate: "idiopathic" sounds learned enough to stifle further inquiry, while "benign" is prognostically too soothing. Despite these handicaps, certain advances in this area worthy of review have developed.

Etiology

It seems clear that so-called idiopathic pericarditis represents a scrapbasket of various undiagnosed types of pericardial disease. Since pericarditis has a somewhat limited clinical repertoire, the specific type cannot be differentiated on clinical grounds alone. Rather, the etiological diagnosis must be sought with the aid of various laboratory disciplines.

Pathological and bacteriological studies have long permitted the recognition of certain specific forms of pericarditis, such as those due to tuberculosis and other bacteria. Pericardial involvement due to fungus infections (e.g., histoplasmosis and toxoplasmosis) has also been reported, based on the evidence of positive skin tests or changing serological titers. In addition, it has long been suspected that many instances of "idiopathic" pericarditis really represented undiagnosed viral infections. Support for this viewpoint has appeared in recent years, with a flood of papers claiming specific viral etiology in cases of so-called "benign idiopathic pericarditis." In particular, the Coxsackie group B viruses have been prominently featured, although other forms of virus have also been implicated (e.g., influenza, mumps, chickenpox, measles, etc.).

It now seems likely that the scrapbasket of "idiopathic" pericarditis can be cleared out to a considerable degree by careful screening for specific forms of infection, particularly those of virus origin. However, the term "viral" pericarditis should be reserved for cases of proven viral origin and should not be used synonymously with "idiopathic" pericarditis. Designating unproven cases as "viral" pericarditis would tend to impede further understanding of either the individual case or the entire group. Instead, it is important to recognize that pericardial involvement can also occur in the absence of specific infection.

Several examples can be cited as evidence for the existence of pericardial disease of apparently noninfectious origin: 1) The frequent occurrence of pericarditis as a manifestation of systemic lupus erythematosus has been well known for years. This suggests that other types of sensitivity reactions, or "collagen-vascular" disorders, could contribute to the group of idiopathic pericarditides. 2) Those of us closely associated with active cardiac surgical programs have been impressed by the clinical similarity between idiopathic pericarditis and the so-called postcommissurotomy syndrome. Some have concluded that this syndrome represents rheumatic activity, which seems unlikely since a similar syndrome also occurs postoperatively in nonrheumatic, congenital heart cases. Rather, it probably represents simple nonspecific pericardial inflammation secondary to surgical trauma, or the collection of irritating products, such as blood, within the pericardial sac. The incidence of this reaction is reduced by surgical techniques permitting adequate pericardial drainage or removing pericardial tissue during cardiac surgery. 3) Several cases of "idiopathic pericarditis" were observed recently during clinical trials of an experimental antibiotic product. This seems to add weight to previous suspicions that the peri-

* From the Edward B. Robinette Foundation for Cardiovascular Research, Medical Clinic, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania.

cardium might "react" to various exogenous or endogenous products, although the exact mechanism of this is not clear. Explanations could include an allergic type of reaction, or even the activation of a latent virus (as in recurrences of herpes simplex). 4) Occasional cases of pericarditis are seen following physical agents, such as radiation treatment or direct trauma to the chest.

With such a wide range of possible causes for "idiopathic" pericarditis, one cannot complacently accept this diagnosis without a careful and extensive search for the underlying factor in each case.

Pathology

Pericardial tissue has been carefully studied by our group in 10 patients with recurrent idiopathic pericarditis who were subjected to operation. Microscopic sections showed only pericardial thickening due to fibrosis, with infiltration of chronic and acute inflammatory cells. Cultures for tuberculosis, fungi, or viruses were entirely negative.

An important observation in certain of the surgical cases was the extension of the process to the underlying myocardium. In one case, the visceral pericardium and myocardium were considerably involved, while the parietal pericardium was relatively spared. Such observations point up the tendency toward combined involvement with the likelihood of a spectrum, ranging from "pure" pericarditis through combinations of varying degrees to "pure" myocarditis.

The observations of Saphir,[1] reported in 1949, are interesting in the light of subsequent developments in the field of virus myocarditis and pericarditis. Many of the recent reports of specific virus infections use the term "myopericarditis" to describe the combined viral involvement. This concept has important implications in the results to be expected from pericardiectomy in such cases. It also helps explain the electrocardiographic variations in patients with pericarditis, since these changes are due to the associated myocardial inflammation.

Clinical Picture

Most patients with idiopathic pericarditis develop an acute febrile illness characterized by chest pains of the so-called pericardial type and distribution. Many describe an antecedent respiratory illness or "virus attack" a week or two earlier. While pain is the major feature, consitutional symptoms with malaise and "grippe-like" sensations are usually present. Symptoms and signs of pleurisy are also common. Objective findings include the characteristic friction rub and electrocardiographic changes, both of which may be quite transient. Usually leucocytosis is present and the sedimentation rate is increased.

The disease is generally referred to as "benign," because it usually subsides without evidence of residual difficulty. In fact, it seems likely that many mild cases remain undetected (e.g., the diagnosis has been made in mildly ill medical colleagues by electrocardiograms which probably would not have been taken under ordinary circumstances). At times, the process is anything but benign, causing severe illness and occasionally death. Pericardial effusions can occur, sometimes requiring paracentesis for the relief of tamponade. The eventual development of pericardial constriction has been the subject of speculation and debate; however, several patients have developed constrictive signs, during a period of personal observation, apparently dating from the original attack. Such cases raise the question of undetected tuberculous pericarditis, but careful studies were completely negative. Thus, it seems likely that "idiopathic" pericarditis can lead to instances of pericardial constriction.

Recurrences of acute idiopathic pericarditis are not common. In most instances, these represent no serious problem, occurring at well-spaced intervals and subsiding promptly on symptomatic treatment. However, certain patients develop recurrent pericarditis that continues as a long, smoldering illness characterized by episodes of severe chest pain, malaise, fever and pleuritis. Each episode subsides relatively promptly on symptomatic treatment and rest. However, exacerbations occur with each attempt to resume normal activity. The result is a pattern of recurrent disability with prolonged or multiple hospitalizations and a state approaching total invalidism. These cases have been described in detail elsewhere.[2-4] They represent a difficult problem in management, although fortunately they constitute only a small percentage of cases.

Diagnosis

The diagnosis of pericarditis may be considered as involving two separate problems: The first is to recognize that pericardial disease is the cause of the difficulty in a given patient. The second is to diagnose the specific cause of pericardial disease.

As a general rule, the diagnosis of acute pericarditis is easily made on clinical grounds alone. The description of the pain is important, especially in respect to the characteristic aggravation by breathing, coughing, rotation of the trunk, or occasionally swallowing. Frequently, the pain radiates widely over the chest, back, shoulders, and particularly into the base of the neck and trapezius region. The characteristic pericardial friction rub should be sought for carefully in such patients. Electrocardiographic changes are usually present and help to confirm the diagnosis. Serial chest films may show

changes in the cardiac silhouette, even when the presence of fluid is not suspected clinically.

Occasionally, the differential diagnosis between acute pericarditis and myocardial infarction may be quite difficult; however, in most instances, the correct diagnosis can be established by careful observation of the course of the illness, with particular reference to serial electrocardiographic changes. Perhaps greater diagnostic difficulty is encountered in those patients with nondescript febrile illnesses in which pain is a less prominent feature. Such patients are considered to have a simple respiratory illness, "virus" infection, pneumonitis, or pleurisy, while the correct diagnosis of pericarditis has not been suspected.

Differential diagnostic problems arise more frequently in those patients who develop pericardial effusion or constrictive pericarditis. Sometimes the diagnosis may be quite easy, as in the presence of pericardial calcification or with clinical and x-ray findings clearly indicative of pericardial effusion. In general, however, recognition of these conditions requires a high index of suspicion that alerts one to consider pericardial disease in all patients who have unexplained congestive failure or elevation of venous pressure. Intensive diagnostic efforts are worth while, since these forms of pericardial disease are potentially curable by surgery. In fact, direct surgical exploration is sometimes justified in certain patients when pericardial constriction cannot be ruled out, despite all diagnostic efforts.

Certain special diagnostic procedures deserve mention. Angiocardiography may be helpful by demonstrating an unopacified area of the cardiac silhouette, particularly along the cardiac border lateral to the right atrium. This technique can show whether or not an enlarged silhouette is due to myocardial dilatation. However, it is a nonspecific test in the sense that the unopacified tissue could consist of exudate, blood, fluid, thickened pericardium, or even tumor. Right atrial pressure curves and electrokymographic records may show distinctive alterations in constrictive pericarditis, but again the changes are nonspecific and occur also in other conditions, such as subendocardial fibroelastosis, which can produce similar hemodynamic effects. Pericardiocentesis can give direct proof of the presence of effusion and can provide fluid for laboratory study. For additional information, the reader is referred to the review of Durant,[5] who discusses the diagnosis of pericardial disease in great detail.

The problem of establishing a definitive etiological diagnosis frequently is more difficult than the initial step of simply recognizing the presence of pericardial disease. One must consider and rule out various diseases elsewhere in the body that are known to produce pericardial manifestations. In ruling out systematic lupus erythematosus, a single negative LE preparation is not adequate, since subsequent tests sometimes may be positive. The skin tests for tuberculosis and the various types of fungi are usually indicated. More recent diagnostic developments include the increased availability of virus laboratories and the extensive use of direct biopsy. Both of these should improve the chances for a specific etiological diagnosis. The importance of seeking a definitive etiological diagnosis cannot be overemphasized. One should not accept a diagnosis of idiopathic pericarditis without expending every effort to rule out specific diseases such as tuberculosis, systemic lupus erythematosus, or even malignant pericardial involvement, all of which can simulate "benign" idiopathic pericarditis.

Treatment

The basic step in treatment is to make every effort to establish a specific diagnosis. When this is not possible, the treatment will depend on the particular stage or type of pericardial syndrome in each individual case.

Treatment during the acute attack usually is symptomatic with bed rest, salicylates, and occasionally narcotics as necessary for control of pain. Broad-spectrum antibiotics have been recommended by some, but one hesitates to use blindly an agent that might mask or alter the course of the disease. This approach is better reserved for cases not following the usual "benign" course. Generally, the patient improves promptly and recovers completely without antibiotics.

In certain patients, the development of pericardial effusion becomes an important consideration. Pericardiocentesis may be done for diagnostic purposes or relief of tamponade. Fluid obtained should be studied for specific infectious agents and tumor cells. Replacement of the fluid with air may be helpful in delineating the thickness of the pericardium and the underlying cardiac size on subsequent x-rays. With recurrent or persistent effusion, the modern approach is to favor early pericardiectomy. This has the advantages of providing adequate tissue for biopsy and culture, while eliminating the adverse effects of compression or tamponade. Surgery at this point is technically easy, as opposed to the difficult dissections encountered later in the course of pericardial disease. The hazards of surgery in undetected tuberculous infections can be avoided by a prophylactic course of antituberculous therapy for 10 or 12 days preoperatively. In resorting to surgery, pericardiectomy seems preferable to the more limited "button biopsy" sometimes used. Drainage "buttons" made during cardiac surgery have sealed off in certain patients, and the more extensive procedure should offer greater protection against future constriction.

Surgery has long been the accepted treatment

in patients with pericardial constriction and should certainly be used, whether the scar is of specific or of idiopathic origin. Here, also, the modern tendency is toward earlier surgery before the patient develops advanced disease with its attendant deleterious effects, particularly deterioration of liver function.

The small group of patients with smoldering, recurrent or subacute pericarditis presents a difficult problem in management. These patients can develop a state of invalidism that does not respond to medical treatment. As reported elsewhere,[2-4] the process has apparently been terminated by pericardiectomy in a small group of carefully selected patients. Naturally, one hesitates to recommend surgery in an ordinarily "benign" disease, but one is forced to this extremity in those patients who fail to respond to all ordinary measures.

Two additional points deserve special mention:

1. Anticoagulants, at times, have been used inadvertently in patients with acute pericarditis because of an erroneous diagnosis of acute coronary occlusion with myocardial infarction. Evidence suggests that anticoagulants may have a deleterious effect in patients with pericarditis, occasionally to the point of producing massive hemopericardium and tamponade. Since hemorrhagic effusion is not uncommon in idiopathic pericarditis, anticoagulants might aggravate the natural process of the disease. In case of diagnostic doubt, it would seem better to omit anticoagulants until a definite diagnosis of coronary occlusion can be made.

2. Steroids have been used to treat pericarditis, particularly in the group of patients with recurrent or subacute disease. Apparently favorable results have been obtained in certain cases. However, steroids were not effective in several of our patients who subsequently recovered following pericardiectomy. This experience has led to a personal preference for surgery rather than the long-term use of steroids. Certainly one should hesitate to use steroids in cases where undetected tuberculosis might easily be present. Moreover, one would also prefer to avoid the problem of long-term steroid therapy with all its worrisome side effects. In good hands, pericardiectomy probably is preferable to the well-documented hazards of long-term steroid therapy.

Summary

1. Idiopathic pericarditis apparently represents a scrapbasket of multiple etiologies.

2. Many of the cases probably are due to undetected virus infections. However, noninfectious causes, such as "collagen-vascular" disease, can also produce pericardial involvement.

3. Proper management requires a careful search for the etiological factor in each case, and one should never be satisfied with a diagnosis of "idiopathic" pericarditis.

4. Diagnostically, the ready availability of virus laboratories and extensive use of biopsies represent recent developments of considerable importance.

5. While the process is usually "benign," an unfavorable course may occur due to pericardial effusion, pericardial constriction, or relapsing, subacute disease.

6. The modern therapeutic approach includes early consideration of surgery in those cases which fail to follow the usual "benign" course, since pericardiectomy can benefit the patient with tamponade, constriction, or prolonged smoldering disease.

HARRY F. ZINSSER, M. D.
Associate Professor of Medicine
University of Pennsylvania
School of Medicine
Philadelphia, Pennsylvania

REFERENCES

1. Saphir, O.: Virus myocarditis. Mod. Concepts Cardiovas. Dis. 18: 43, 1949.
2. Zinsser, H. F.: Pericardiectomy for recurrent idiopathic pericarditis in the absence of significant cardiac constriction. Tr. Am. Clin. and Climatol. A. 69: 40, 1957 (1958).
3. Zinsser, H. F., Johnson, J., and Blakemore, W. S.: Concept of pericardiectomy as a treatment for recurrent idiopathic pericarditis in the absence of cardiac constriction. Am. J. Med. Sc.. 238: 464, 1959.
4. Zinsser, H. F., Blakemore, W. S., Kirby, C. K., and Johnson, J.: Invalidism due to recurrent idiopathic pericarditis with recovery after pericardiectomy. J.A.M.A. 171: 274, 1959.
5. Durant, T. M.: Recognition of pericardial disease. Mod. Concepts Cardiovas. Dis. 27: 455, 1958.